### **ADVANCES IN HEPATOLOGY**

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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## Transaminase Levels and Vigorous Exercise

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## **G&H** Why are levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) monitored in patients with chronic liver disease?

MS Clinicians monitor transaminase enzymes because they are good markers of the inflammation that may impair liver function. When we see abnormal transaminases, we think of liver disease. However, raised levels of transaminases do not discriminate amongst the various disease states. Once raised levels have been detected, it is necessary to pinpoint what is causing the abnormality.

#### **G&H** How are liver dysfunction and vigorous exercise both linked to raised transaminase levels?

MS Healthy individuals have normal levels of transaminase enzymes. Although the levels that constitute "normal" are currently under debate, most people who are healthy have levels that are recognizably within the normal range.

However, just as these markers do not discriminate among liver diseases, they do not discriminate among several different sources of inflammation. Thus, raised levels can be traced to muscular inflammation as well as hepatic inflammation. People who exercise heavily (eg, weight lifters, marathon runners, soldiers who perform heavy-duty labor) can have abnormal transaminase levels, as can those suffering muscular trauma, such as myocardial infarction or even surgery in which some muscles are cut. The normal repair process in these cases engenders inflammation and raises transaminase levels.

#### **G&H** Do ALT and AST react to hepatic and muscular inflammation similarly?

**MS** Basically, the reaction between the two is similar. Again, there is a ratio that in healthy individuals is considered normal. AST levels normally measure at approximately 0.8 of ALT levels. A dysregularity of this ratio can also signal hepatic illness but usually inflammation of any kind affects both measures.

## **G&H** Can exercise-related elevations be correlated to individual incidences of exercise or muscle exertion, or do they build over time?

**MS** Publications on the subject have documented that once enzymes are abnormal, they remain abnormal for up to 1 week. Were subjects to exercise vigorously again during that week, transaminase levels could increase further. Some of the abnormalities have been noted as significant, particularly in marathon runners.

# **G&H** Is it possible to raise transaminase levels with aerobic exercise, or does elevation only occur in conjunction with strength training or manual labor?

MS Strength training and very heavy manual labor are a much more likely cause of raised levels than aerobic exercise. Marathon running is an extreme form of aerobic exercise, but I would not classify it similarly. Although there are not many studies on aerobic exercise, shorter treadmill runs do not produce the abnormalities that occur in people who run 26 miles or more. Marathon runners have the potential to seriously damage their muscles through a process called rhabdomyolysis, which can raise transaminase levels significantly.

#### **G&H** Are exercise-induced levels of transaminases ever a cause for concern?

MS Concern would depend on the level of abnormality. In general, it is good for patients with liver disease to exercise, particularly those with fatty liver disease. In fact, we see a trend toward improved ALT and AST levels in patients performing moderate exercise, regardless of the etiology of their liver disease. We therefore discourage very heavy exercise in these patients, but a moderate amount does not cause a problem.

**G&H** What are the highest levels of transaminases that could be attributed to vigorous exercise? At what level should physicians begin looking for another cause?

**MS** We accept 1–2 times the upper limit of normal to be attributable to exercise or to certain medications such as cholesterol-lowering drugs. Beyond this level, there should definitely be concern of a clinically significant hepatic condition.

**G&H** What challenges do exercise-induced transaminase increases present to treating physicians?

MS Some physicians, whether they are gastroenterologists or internists, forget that exercise can cause this abnormality. I have received referrals in the liver-disease clinic for a perfectly healthy person who happens to be exercising, whose history has not been taken or is not believed by the physician. This referral can lead to resources wasted on patients who have no illness and no other symptoms beyond these raised transaminase levels.

It is important to question patients about their exercise history, particularly if they have recently started a new regime. If a patient has just started lifting weights, there will be some associated muscle injury, as opposed to the ongoing conditioning of a regular exerciser.

#### **Suggested Reading**

Pettersson J, Hindorf U, Persson P, Bengtsson T, Malmqvist U, et al. Muscular exercise can cause highly pathological liver function tests in healthy men. *Br J Clin Pharmacol.* 2007 Aug 31; [Epub ahead of print]

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Suzuki A, Lindor K, St Saver J, Lymp J, Mendes F, et al. Effect of changes on body weight and lifestyle in nonalcoholic fatty liver disease. *J Hepatol.* 2005;43:1060-

Fallon KE, Sivyer G, Sivyer K, Dare A. The biochemistry of runners in a 1600 km ultramarathon. *Br J Sports Med.* 1999;33:264-269.